Case Report

A rare case of sarcoidosis with necrotizing mediastinal lymphadenitis misdiagnosed as multidrug-resistant tuberculosis (MDR- TB)

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ABSTRACT

Sarcoidosis, a multisystem disorder of unknown cause, is characterized by the presence of non-caseating granulomas and the proliferation of epithelioid cells. Sarcoidosis mostly affects the lungs and mediastinal lymph nodes in 90% of cases. Caseation and necrosis are very rare. We report the present case in view of its rarity, as sarcoidosis with significant necrosis in mediastinal lymph nodes is a rare phenomenon and can mislead the treating physician into diagnosing it as tuberculosis, which can lead to exposure of the patient to undue side effects of anti-tubercular drugs.

KEY WORDS: Multidrug resistant tuberculosis (MDR- TB), necrotizing mediastinal lymphadenopathy, sarcoidosis

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INTRODUCTION

Sarcoidosis, a multisystem disorder of unknown cause, is characterized by the presence of non-caseating granulomas and the proliferation of epithelioid cells.[1] In general, sarcoidosis mostly affects young adults, with a slightly higher prevalence in females.[2] The lungs and mediastinal lymph nodes are involved in over 90% of cases with thoracic sarcoidosis, which reasonably explains the record morbidity and mortality.[3] Hilar and mediastinal lymphadenopathy are conjoint manifestations of sarcoidosis and may be seen as distinguished abnormality in combination with parenchymal disease. The lymphadenopathy is characteristically symmetrical in distribution. Non-necrotizing granulomas are distinctive histological findings of sarcoidosis, but necrosis or cavitation is rare and is seen in less than 1% of patients.[4] Here, we report a rare case of sarcoidosis with necrotizing mediastinal lymph nodes misdiagnosed as multidrug-resistant tuberculosis (MDR-TB) which responded to oral corticosteroids and showed significant clinico-radiological improvement with no recurrence of disease on follow up.

CASE REPORT

A 27-year-old female presented with complaints of dry cough, low grade fever for two years and nodular skin lesions for six months. Past history revealed anti-tubercular treatment (ATT). Initially, she was started on isoniazid + rifampicin + pyrazinamide + ethambutol (HRZE) for two months followed by isoniazid + rifampicin + ethambutol (HRE)

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in continuation phase at adequate doses on the basis of clinical and contrast enhanced computed tomography (CECT) chest findings for a total duration of nine months. There was no response to treatment. The patient was then started on category II (CAT II) regimen comprising of isoniazid + rifampicin + pyrazinamide + ethambutol + streptomycin (HRZES), which was continued for a total duration of two months only, after which the patient was investigated and was treated for MDR-TB (moxifloxacin 400 mg, cycloserine 500 mg, ethionamide 500 mg, pyrazinamide 1500 mg, ethambutol 800 mg with injection of kanamycin 0.75 g daily) for six months. MDR-TB was confirmed on GeneXpert report on bronchoalveolar lavage fluid (BAL) that showed *Mycobacterium tuberculosis* and rifampicin resistance. Endobronchial ultrasound-guided transbronchial needle aspiration (TBNA) specimen was sent for MGIT 960 culture for *Mycobacterium tuberculosis* and was found to be negative after seven weeks of incubation. However, MDR regimen was continued, and there was no response even after 14 months of treatment. Instead, she developed adverse drug reactions like joint pain, hyperuricemia and hypothyroidism.

Complete blood count, hepatic and renal function tests were within normal limits. Serum uric acid was significantly raised at 15.9 mg/dL and thyroid stimulating hormone was 15 μIU/mL. Chest X-ray showed bilateral hilar lymphadenopathy [Figure 1]. CECT of the chest done 14 months prior MDR-TB treatment initiation showed necrosis in the lymph nodes of the mediastinal window [Figure 2]. Follow-up CECT of the chest after 14 months of MDR-TB treatment showed multiple large necrotic nodes (15.5 mm) in the right para-tracheal region, left para-tracheal region (13 mm), left hilar (16 mm), right hilar (12 mm) and subcarinal (14 mm) [Figure 3]. Endobronchial ultrasound-guided TBNA from mediastinal lymph nodes was done. TBNA specimen was sent for MGIT 960 culture for *M. tuberculosis* and was found to be negative after seven weeks of incubation. Mantoux test was negative. Serum for angiotensin converting enzyme (ACE) was 62.8 U/L, total urinary calcium was 212.94 mg/24 hours, and serum calcium was 10.92 mg/dL. Histopathological examination of biopsy from the skin nodules revealed dermis with a fair number of vaguely formed epithelioid granuloma surrounded by mixed inflammatory infiltrates with some amount of necrosis, suggestive of sarcoidosis [Figure 4]. Ophthalmic examination was normal. Ultrasound examination of whole abdomen showed no evidence of any retroperitoneal lymphadenopathy and hepatosplenomegaly. Anti-tubercular treatment was stopped with immediate effect after the biopsy report. The patient was started on prednisolone 40 mg daily on the basis of histopathological examination of the biopsy specimen from the skin nodule. After initiation of oral corticosteroids, skin lesions subsided drastically with the resolution of other chest symptoms [Figure 5a and 5b]. CECT chest showed significant regression in the size of mediastinal lymph nodes after two months of treatment with corticosteroids [Figure 6]. The dose of prednisolone was tapered rapidly due to remarkable steroid-induced weight gain. She was continued with 5 mg prednisolone on alternate days thereafter as maintenance dose. Follow up of the patient in the next three years showed no recurrence of the disease.

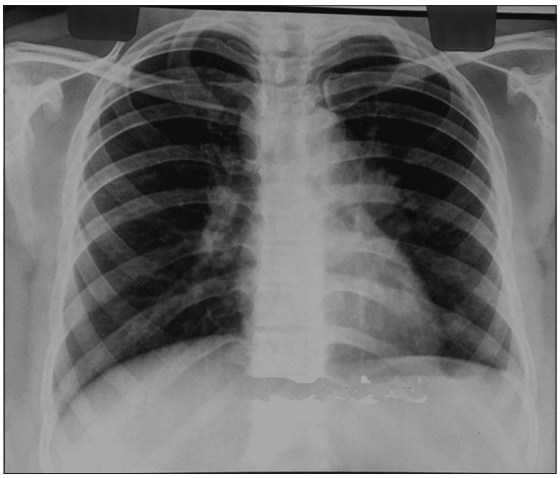

Figure 1: Chest X-ray showing bilateral hilar lymphadenopathy

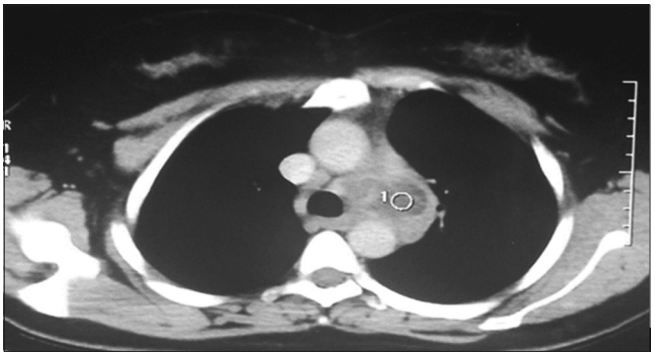

Figure 2: CECT of chest (mediastinal window) 14 months prior to MDR treatment showing necrosis in the lymph nodes in the mediastinal window

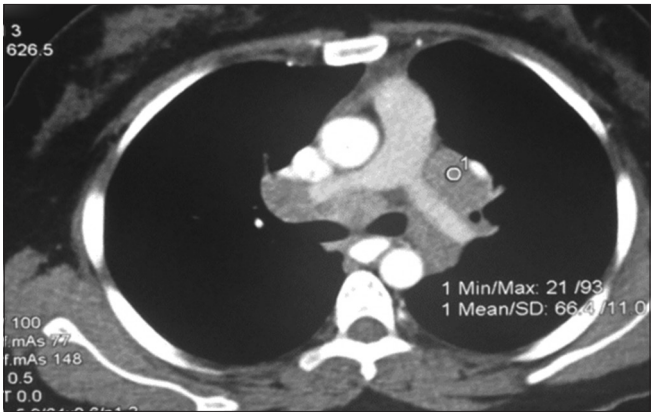

Figure 3: Follow-up CECT of chest, done after 14 months of treatment for MDR-TB, showing multiple large necrotic lymph nodes in the mediastinal window

DISCUSSION

Sarcoidosis, a multisystem disorder of unknown cause, is characterized by the presence of non-caseating granulomas and the proliferation of epithelioid cells.[1] In general, sarcoidosis mostly affects young adults, with a slightly higher prevalence in females.[2] The lungs and mediastinal lymph nodes are involved in over 90% of cases with thoracic sarcoidosis, which reasonably explains the record morbidity and mortality.[3] Hilar and mediastinal lymphadenopathy are conjoint manifestations of sarcoidosis and may be seen as distinguished abnormalities in combination with parenchymal disease. The lymphadenopathy is characteristically symmetrical in distribution, with involvement of hilar, para-tracheal, aorto-pulmonary window and sub-carinal region. Non-necrotizing granulomas are a distinctive, histological finding of sarcoidosis, but necrosis or cavitation occurs in less than 1% of patients. Diagnosis of sarcoidosis is established on compatible clinical and radiological findings with histological finding of non-caseating epithelioid cell granulomas and the elimination of other granulomatous diseases.[4,5] However, in our case, substantial necrosis was evident in the mediastinal lymph nodes on computed tomography (CT) of the thorax. Rockoff and Rohtagi, in a systematic review, described the relative incidence and classification of uncommon thoracic manifestations of sarcoidosis.[6] Karkhanis and Joshi reported a case of parotid swelling, provisionally diagnosed as tuberculous inflammation in view of granuloma showing caseous necrosis on cytology, which was diagnosed as sarcoidosis thereafter. CT thorax showed homogenously enhancing mediastinal lymph nodes.[7] Dhooria *et al*.[8] compared endobronchial ultrasound appearances of lymph nodes in patients with tuberculosis and sarcoidosis and concluded that heterogeneous echotexture and coagulation necrosis sign in lymph nodes favored a diagnosis of tuberculosis over sarcoidosis. This finding was dissimilar to ours in which sarcoidosis presented with necrosis in mediastinal lymph nodes.[9] GeneXpert assays play an essential role in the diagnosis of tuberculosis (TB), with overall good sensitivity and excellent specificity. The role of GeneXpert assays in diagnosing reinfection or relapse has not yet been fully explained. Theron *et al*.[10] reported that after the completion of the appropriate treatment, GeneXpert can produce false-positive results for up to four years and in 8.72% of positive tests on respiratory samples, for up to 18 months, possibly due to both the presence of residual mycobacterial DNA in the respiratory tract and the detection of non-viable bacilli.[11] False-positive results of MTB smears, cultures, or molecular tests in bronchoscopically obtained samples are mainly due to cross-contamination owing to inadequate decontamination of bronchoscopes between use[12] or cross-contamination in the laboratory.[13] Xpert MTB/RIF (Cepheid) is a closed system which reduces the risk of cross-contamination. Therefore false-positive Xpert results after bronchoscopically obtained samples are possibly due to a result of inadequate decontamination of the bronchoscope. Thus, in our case, GeneXpert showed false positive results which led to misdiagnosing a sarcoidosis case as rifampicin-resistant (RR) TB.

CONCLUSION

Sarcoidosis mostly affects lungs and mediastinal lymph nodes in 90% of cases. Caseation and necrosis are very rare. However, in the above case, it can be concluded that significant necrosis in mediastinal lymph nodes despite being rare can be sarcoidosis and can mislead the treating physician into diagnosing it as tuberculosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the

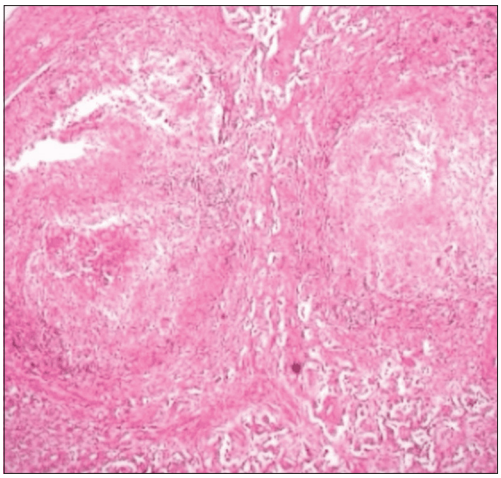

Figure 4: Dermis with fair number of vaguely formed epithelioid granuloma surrounded by mixed inflammatory infiltrates with some amount of necrosis suggestive of sarcoidosis

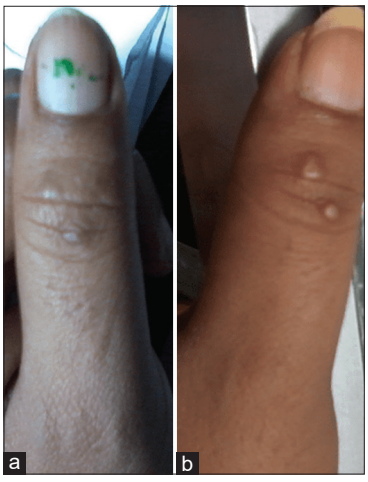

Figure 5: Skin lesion before treatment initiation (5a) and skin lesions after oral corticosteroid treatment (5b)

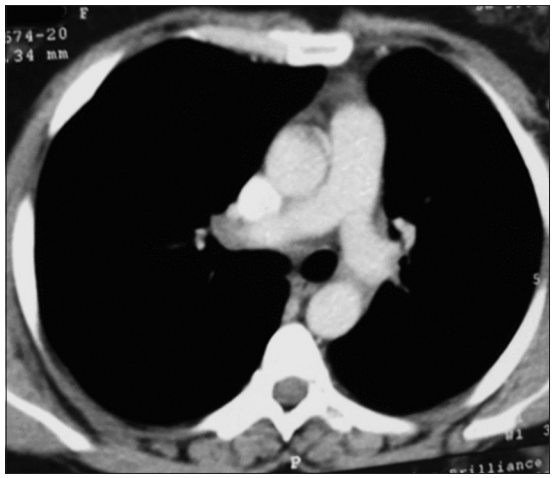

Figure 6: Follow-up CECT of chest done two months after treatment with oral corticosteroids showing significant regression in the size of the mediastinal lymph nodes

patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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